REMARKS

The Office Action of October 14, 2003 has been received and carefully reviewed. It is submitted that, by this Amendment, all bases of rejection and objection are traversed and overcome. Upon entry of this Amendment, Claims 1-21 remain in the application. New claims 22-25 have been added in order to set forth additional specific embodiments of Applicants' invention.

Claims 1-21 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically regarding claim 1, the Examiner points out that "micro-tubular" and "oriented architecture" are uncertain as to meaning and scope in relation to defining the material obtained. Further, the Examiner states that it is unclear how micro-tubular differs from porous, and as to the structure required by having an oriented architecture. Still further, the Examiner states that "directional temperature gradient" is uncertain as to meaning and how the limitation defines the temperature used. The Examiner further states that "unnecessary phase" is uncertain as to meaning and scope and that being "unnecessary" is relative and subjective, and it would be uncertain as to when a phase is necessary and not necessary.

Claim 1 has been revised to recite that the phase separation forms a first and second phase, and that the first phase is removed. Claim 1 further has been revised to recite that the directional temperature gradient extends along a predetermined axis from a first region of the composition at a second temperature to a second region of the composition at a third temperature. Further, claim 1 has been revised to recite that the micro-tubular polymeric materials comprise a plurality of micro-tubules having a predetermined architecture with each of the plurality of micro-tubules arranged substantially parallel to each other. It is submitted that the revisions to claim 1 are fully supported by the application as filed. For example, one non-limitative description of the directional temperature gradient appears at page 9, paragraph 51. One non-limitative description of the parallel orientation of the micro-tubules appears at page 8, paragraph 47. Claim 17 has also been amended to recite that the "first" phase is removed.

As such, Applicants respectfully submit that the rejection under 35 U.S.C. 112, second paragraph of claim 1 and those claims depending therefrom has been traversed and overcome.

Claims 20 and 21 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

Applicants regard as the invention. The Examiner states that the claims are confusing by requiring a composition formed by the method of claim 1 since claim 1 does not recite "composition."

Claims 20 and 21 have been revised to recite "materials" as recited in claim 1. As such, Applicants respectfully submit that the rejection of claim 20 and 21 under 35 U.S.C. 112, second paragraph, has been traversed and overcome.

Claims 1, 2, 7-9, and 13-20 stand rejected under 35 USC 102(b) as being anticipated by Zhang et al (1999). The Examiner states that Zhang discloses producing poly(α-hydroxyl acids)/hydroxyapatite porous composite foams by forming a solution containing PLLA or PLGA and hydroxyapatite (HAP), changing the temperature to cause phase separation and removing an unnecessary phase by freezing and drying. Further, the Examiner asserts that Zhang discloses that a PLLA foam is produced by solid-liquid phase separation by the procedure used to produce the composite except that HAP is not present. Still further, the Examiner asserts that the Zhang PLLA foam has an anisotropic tubular morphology with an internal ladder-like structure and parallel channels with each channel having repeated partitions with uniform spacing as shown in Zhang's Fig. 1(d). The Examiner concludes that there is no apparent step and/or condition in the present specification and claims that is different than that disclosed by Zhang that would have produced a structure different than Zhang's Fig. 1(d). The Examiner further asserts, contrary to the description in the instant specification, that Zhang's Fig. 1(d) shows an oriented architecture uniformly throughout the PLLA foam.

Applicants respectfully submit that Zhang does not teach or suggest use of a directional temperature gradient as in Applicants' invention as defined in claim 1. Zhang discloses that the mixture is prepared in a pre-warmed beaker and is then transferred into a preset refrigerator or freezer.

In contrast, the Applicants' invention as defined in amended claim 1 recites the use of a directional temperature gradient which extends along a predetermined axis from a first region of the composition at a second temperature to a second region of the composition at a third temperature. The Examiner is directed to the Applicants' specification at page 9, lines 8-13, which states:

> For the oriented micro-tubular scaffolds, the phase separation was carried out with a uni-axial temperature gradient. To achieve this directional temperature gradient, the beaker side was wrapped with a layer of thermal

> insulating material to reduce the heat transfer through the side wall, and the beaker was set on top of a block of metal in a freezer to increase the heat conduction along the longitudinal direction.

Further, Zhang states that, "[p]hase-separation temperature does not show obvious effects on the porosity of the polymer/HAP foams in the composition range studied." Page 448, 1st column under "Results."

In sharp contrast, the Examiner is directed to the Applicants' specification at page 12, lines 1-5, which recites:

> when a temperature gradient was maintained uniaxially during the thermally induced phase-separation process, the characteristic architecture of an array of parallel micro-tubules was achieved (Figure 1 a-e and g-i). When the temperature gradient was not uni-axial, the pore architecture was randomly oriented (Figure 1f).

Further, Applicants direct the Examiner to the attached Declaration pursuant to 37 C.F.R. 1.132 with attached Exhibit 1. The Declaration states that Zhang's Figure 1(d) is a section of a PLLA foam prepared from the 2.5% (w/v) PLLA/dioxane solution (quenching temperature: -18°C). The Declaration further states that Exhibit 1 is a SEM of a section of a PLLA foam prepared from the 2.5% (w/v) PLLA/dioxane solution (quenching temperature: -18°C) (the same materials, solvent and conditions that formed the foam of Zhang/Ma Figure 1d).

Zhang's Figure 1(d) does not depict "an oriented architecture uniformly throughout the PLLA foam," as asserted by the Examiner, rather it shows a *portion* of the foam having substantially locally oriented parallel pores. Exhibit 1 is a portion of a foam (formed from the same materials and in the same manner as the foam shown in Zhang Figure 1d) illustrating that the pores are not parallel, but rather have a random orientation. Exhibit 1 shows that a PLLA foam prepared as disclosed by Zhang does not have a uniform architecture throughout. Examining Zhang's Figure 1d and Exhibit 1 together, Applicants submit that PLLA foam disclosed by Zhang has portions that are randomly oriented, portions that are parallel, and still other portions that are parallel, but not parallel to other parallel portions.

In sharp contrast, Applicants' invention as defined in claim 1 recites having a predetermined architecture with each of the plurality of micro-tubules arranged substantially

parallel to each other, substantially uniformly throughout the materials. As shown in Applicants' Figures 1a-1d, each tubule is parallel to the next. As stated in the attached Declaration:

> After reviewing Figure 1d of the Zhang/Ma 1999 reference and Exhibit 1, I submit that the substantially parallel oriented pores of Figure 1d are a portion of the entire PLLA foam. Other portions of that foam were also locally oriented, but not parallel to the portion shown in Figure 1d. Still other portions were randomly oriented, similar to that shown in Exhibit 1.

As such, it is submitted that the Zhang/Ma 1999 reference does not teach or suggest materials having microtubles parallel to each other substantially uniformly throughout the materials as recited in Applicants' invention as defined in claim 1.

For all the reasons stated above, it is submitted that Applicants' invention as defined in claims 1, 2, 7-9, and 13-20 is not anticipated, taught or rendered obvious by Zhang et al (1999), and patentably defines over the art of record.

The remaining pending claims depend ultimately from claim 1. It is submitted that, through this dependency, Applicants' invention as defined in these claims also is not anticipated, taught or rendered obvious by Zhang et al (1999), and patentably defines over the art of record.

Claims 3-6 and 21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. The Examiner states that it would have been obvious to seed cells on the PLLA foam taught by Zhang and culture the cells for tissue engineering since this is a known use for a tissue engineering scaffold made from PPLA.

Due to the randomly oriented pores as described in Zhang, discussed above, cells would be randomly distributed in the porous matrix.

In sharp contrast, Applicants' invention as defined in claims 3-6 and 21 recites seeding cells on a material having "micro-tubules having a predetermined architecture with each of the plurality of micro-tubules arranged substantially parallel to each other" (as defined in claim 1). Due to Applicants' structure, the cells grow and follow the geometric cues of the parallel tubular architecture. The Examiner is directed to the Applicants' specification at page 15, line 5, which states in part that, "cell distribution followed the architectural features." As a result, seeding cells on parallel oriented tubules as defined by Applicants would not have been obvious in view of the substantially non-uniformly oriented foam disclosed in the Zhang reference.

For all the reasons stated above, it is submitted that Applicants' invention as defined in claims claims 3-6 and 21 is not anticipated, taught or rendered obvious by the cited references, either alone or in combination, and patentably defines over the art of record.

Claims 1-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (1999) in view of Ma et al. and Vacanti et al. (US Pat. No. 6,348,069). The Examiner states that Ma et al. disclose adding a polymer to a liquid, changing the temperature to cause phase separation and removing an unnecessary phase to obtain a porous matrix for use as a scaffold in tissue engineering. Further, the Examiner points out that Vacanti et al. discloses forming a polymeric (PLGA) matrix scaffold for seeding with cells and implanting to form tissue. The Examiner argues that it would have been obvious to omit HAP from the steps of Zhang and carry out a process the process to produce a structure as shown in Zhang's Figure 1(d) as suggested by Ma. The Examiner continues stating that Vacanti would have further suggested omitting HAP from a scaffold formed only from PLGA and that he clearly suggested seeding the PLLA or PLGA foam with cells and culturing. The Examiner points out that the polymers as listed in claim 10-12 are alternatives to PLGA for making a scaffold as disclosed by Vacanti, and that the use of these polymers would have been obvious.

The Applicants point out that, as previously discussed, the material as defined by Applicants' claim 1 (shown in Figures 1a-1d) does not have the same pore structure as shown in Zhang's Figure 1(d). Therefore, it is submitted that Ma's suggestion to remove HAP to obtain Zhang's structure (as asserted by the Examiner) is irrelevant to the Applicants' invention as defined in claim 1 and shown in Figures 1a-1d.

Furthermore, Ma does not disclose the use of a directional temperature gradient during matrix fabrication.

Applicants respectfully submit that Vacanti teaches and suggests the use of polymers having fibrous structures – meaning "one or more fibers that is entwined with itself, multiple fibers in a woven or non-woven mesh, and sponge like devices." (Col. 3, lines 50-51).

In sharp contrast, Applicants invention as defined in claim 1 is not a fibrous structure.

Regarding Vacanti, Applicants further submit that he discloses a single tube for vascular structures. Vacanti teaches individual tubular constructs having a length of 2 cm and a diameter of 0.8 cm. Col. 8, lines 40-45.

In sharp contrast, Applicants' invention as defined in claims 22 and 24 recites a plurality of micro-tubules having diameters as small as 2 microns and as large as 200 microns.

For all the reasons stated above, it is submitted that Applicants' invention as defined in claims claims 1-21 is not anticipated, taught or rendered obvious by the cited references, either alone or in combination, and patentably defines over the art of record.

In summary, claims 1-21 remain in the application. New claims 22-25 have been added in order to set forth additional specific embodiments of Applicants' invention. It is submitted that, through this amendment, Applicants' invention as set forth in these claims is now in a condition suitable for allowance.

Further and favorable consideration is requested. If the Examiner believes it would expedite prosecution of the above-identified application, he is cordially invited to contact Applicants' Attorney at the below-listed telephone number.

Respectfully submitted,

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